#3

FORM PTO-1449 (Modified [6-1])

LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT(S)' INFORMATION DISCLOSURE STATEMENT
(Use several sheets if necessary)

ATTY. DOCKET NO.	SERIAL NO.
23623-7078	~~Not Assigned~~

jc872 U.S. PTO 10/075907 02/12/02

INVENTOR
Davis et al.

FILING DATE	GROUP ART UNIT
~~Herewith~~	~~Not Assigned~~ 1652

REFERENCE DESIGNATION **U.S. PATENT DOCUMENTS**

EXAM'R INITIAL		DOCUMENT NUMBER	DATE	NAME	Class	Subclass	Filing Date If Appropriate
ES	*A1	5,208,158	05/04/93	Bech et al.			
	*A2	5,244,791	09/14/93	Estell			
	*A3	5,316,935	05/31/94	Arnold et al.			
	*A4	5,316,941	05/31/94	Estell et al.			
	*A5	5,403,737	04/04/95	Abrahmsen et al.			
ES	*A6	5,629,173	05/13/97	Abrahmsen et al.			

FOREIGN PATENT DOCUMENTS

EXAM'R INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	Subclass	TRANSLAT'N
ES	*B1	WO 91/16423	04/18/91	PCT			yes
ES	*B2	WO 96/27671	02/27/96	PCT			yes
ES	*B3	EP 3 328 229 A1	08/1989	EP			yes
ES	*B4	WO 97/37007	10/09/97	PCT			yes
ES	*B5	WO 98/23732	06/04/98	PCT			yes

ES

OTHER ART (Include Author, Title, Date, Pertinent Pages, *etc.*)

ES	*C1	Akabas et al., "Acetylcholine Receptor Channel Structure Probed in Cysteine- Substitution Mutants," Science, 258:307-310 (1992)
	*C2	Alvear et al., "Inactivation of Chicken Liver Mevalonate 5-Diphosphate Decarboxylase by Sulfhydrl-Directed Reagents: Evidence of a Functional Dithiol," Biochimica et Biophysica Acta, 994:7-11 (1989)
	*C3	Bech, et al., "Chemical modifications of a cysteinyl residue introduced in the binding site of carboxypeptidase y by site-directed mutagenesis.", Carlsberg Res. commun., 53:381-393 (1988)
	*C4	Bech et al., "Significance of Hydrophobic S_4-P_4 Interactions in Subtilisin 309 from *Bacillus Lentus,*" Biochemistry, 32:2847-2852 (1993)
	*C5	Bell et al., "Kinetic Studies on the Peroxidase Activity of Selenosubtilisin," Biochemistry, 32:3754-3762 (1993)
	*C6	Berglund et al., "Chemical Modification of Cysteine Mutants of Subtillisin *Bacillus Lentus* Can Create Better Catalysts Than The Wild-Type Enzyme," J. Am. Chem. Soc., 119:5265-5266 (1997)
	*C7	Berglund, et al., Altering the specificity of subtilisin B. Llentus by combining site-directed mutagenesis and chemical modification," Bioorganic & Medicinal Chemistry Letters, 6:2507-2512 (1996)
	*C8	Bodwell et al., "Sulfhydryl-Modifying Reagents Reversibly Inhibit Binding of Glucocorticoid-Receptor Complexes to DNA-Cellulose," Biochemistry, 23:1392-1398 (1984)
	*C9	Bonneau et al., "Alteration of the Specificity of Subtilisin BPN' by Site Directed Mutagenesis in Its S_1 and S_1' Binding Sites," J. Am. Chem. Soc., 113:1026-1030 (1991)
	*C10	Brocklehurst, "Specific Covalent Modification of Thiols: Applications in the Study of Enzymes and Other Biomolecules," Int. J. Biochem., 10:259-274 (1979)
ES	*C11	Bruice et al., "Novel Alkyl Alkanethiolsulfonate Sulfhydryl Reagents. Modification of Derivatives of L-Cysteine," Journal of Protein Chemistry, 1:47-58 (1982)

EXAMINER S. Slobodyanskaya | DATE CONSIDERED 8/19/03

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	INVENTOR Davis et al.	
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ES	*C12	Buckwalter, et al., "Improvement in the Solution Stability of Porcine Somatotropin by Chemical Modification of Cysteine Residues," J. Agric. Food Chem., 40:356-362 (1992)
	*C13	Daly et al., "Formation of Mixed Disulfide Adducts at Cysteine-281 of the Lactose Repressor Protein Affects Operator And Inducer Binding Parameters," Biochemistry, 25:5468-5474 (1986)
	*C14	Davies et al., "A Semisynthetic Metalloenzyme Based on a Protein Cavity That Catalyzes the Enantioselective Hydrolysis of Ester and Amide Substrates," J. Am. Chem. Soc., 119:11643-11652 (1997)
	**C15	Davis, B.G., et al., "Altering the specificity of subtilisin Bacillus lentus through the introduction of positive charge at single amino acid sites," Bioorganic and Medicinal Chemistry, (1999 Nov.) 7(11) 2303-11, XPO000892841
	**C16	Davis, B.G., et al., "The controlled introduction of multiple negative charge at single amino acid sites in subtilisin bacillus lentus," Bioorganic and Medicinal Chemistry, (1999 Nov.) 7(11) 2293-301, XPO000892840.
	**C17	Desantis, G., et al, "Probing the altered specificity and catalytic properties of mutant subtilisin chemically modified at position S156C and S166C in the S1 pocket," Bioorganic and Medicinal Chemistry, (1999) 7/7 (1381-1387), XP0000892843
	*C18	Desantis, G., et al., "Chemical Modifications at a single site can induce significant shifts in the pH profiles of a serine protease," J. Am. Chem. Soc.,, 120:8582-8586 (1998)
	*C19	Desantis, G., et al., "Site-Directed Mutagenesis combined with chemical modification as a strategy for altering the specificity of the S1 and S1' pockets of subtilisin bacillus lentus," Biochemistry, 37: 5968:5973 (1998)
	*C20	Di Bello, "Total Synthesis of Proteins by Chemical Methods: The Horse Heart Cytochrome C Example," Gazzetta Chimica Italiana, 126:189-197 (1996)
	**C21	Dickman, M., et al., "Chemically modified mutants of subtilisin bacillus lentus catalyze transesterification reactions better than wild type," Tetrahedron Asymmetry, (11. Dec. 1998) 9/23 4099-4102, XPO000891276.
	*C22	Engler et al., "Critical Functional Requirement for the Guanidinium Group of the Arginine 41 Side Chain of Human Epidermal Growth Factor as Revealed by Mutagenic Inactivation and Chemical Reactivation," The Journal of Biological Chemistry, 267:2274-2281 (1992)
	*C23	Frillingos, et al., "Cysteine-Scanning Mutagenesis of Helix II and Flanking Hydrophilic Domains in the Lactose Permease of *Escherichia coli*," Biochemistry, 36:269-273 (1997)
	*C24	Gloss et al., "Examining the Structural and Chemical Flexibility of the Active Site Base, Lys-258, of *Escherichia coli* Aspartate Aminotransferase by Replacement with Unnatural Amino Acids," Biochemistry, 34: 12323-12332 (1995)
	*C25	Gron et al., "A Highly Active and Oxidation-Resistant Subtilisin-Like Enzyme Produced by a Combination of Site-Directed Mutagenesis and Chemical Modification," Eur. J. Biochem., 194:897-901 (1990)
	*C26	Hempel et al., "Selective Chemical Modification of Human Liver Aldehyde Dehydrogenases E_1 and E_2 by Iodoacetamide," The Journal of Biological Chemistry, 256:10889-10896 (1981)
ES	*C27	Hilvert et al., "A Highly Active Thermophilic Semisynthetic Flavoenzyme," J. Am. Chem. Soc., 110:682-689 (1988)

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INVENTOR: Davis et al.	
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	*C28	Hilvert et al., "New Semisynthetic Flavoenzymes Based on a Tetrameric Protein Template, Glyceraldehyde-3-Phosphate Dehydrogenase," J. Am. Chem. Soc., 107:5805-5806 (1985)
	*C29	House et al., "^{1}H NMR Spectroscopic Studies of Selenosubtilisin," Biochemistry, 32:3468-3473 (1993)
	*C30	Huang et al., "Improving the Activity of Immobilized Subtilisin by Site-Specific Attachment to Surfaces," Anal. Chem., 69:4601-4607 (1997)
	*C31	International Search Report, mailed July 21, 2000, Corresponding PCT US99/30362
	*C32	Kaiser, "Catalytic Activity of Enzymes Altered at Their Active Sites," Angew. Chem. Int. Ed. Engl., 27:913-922 (1988)
	*C33	Kanaya et al., "Role of Cysteine Residues in Ribonuclease H from *Escherichia coli,*" Biochem. J., 271:59-66 (1990)
	*C34	Kawase et al., "Effect of Chemical Modification of Tyrosine Residues on Activities of Bacterial Lipase," Journal of Fermentation and Bioengineering, 72:317-319 (1991)
	*C35	Kenyon, et al., "Novel Sulfhydryl Reagents," Methods Enzymol., 47:407-430 (1977)
	*C36	Kirley, "Reduction and Fluorescent Labeling of Cyst(e)ine-Containing Proteins for Subsequent Structure Analyses," Analytical Biochemistry, 180:231-236 (1989)
	*C37	Kluger et al., "Amino Group Reactions of the Sulfhydryl Reagent Methyl Methanesulfonothioate. Inactivation of D-3-hydroxybutyrate Dehydrogenase and Reaction with Amines in Water," Can. J. Biochem, 58:629-632 (1980)
	*C38	Kokubo et al., "Flavohemoglobin: A Semisynthetic Hydroxylase Acting in the Absence of Reductase," J. Am. Chem. Soc., 109:606-607 (1987)
	*C39	Konigsberg, "Reduction of Disulfide Bonds in Proteins with Dithiothreitol," Methods in Enzymology, 25:185-188 (1972)
	*C40	Kuang et al., "Enantioselective Reductive Amination of *a*-Amino Acids by a Pyridoxamine Cofactor in A Protein Cavity," J. Am. Chem. Soc., 118:10702-10706 (1996)
	*C41	Lewis et al., "Determination of Interactive Thiol Ionizations in Bovine Serum Albumin, Glutathione, and Other Thiols by Potentiometric Difference Titration," Biochemistry, 19:6129-6137 (1980)
	*C42	Liu et al., "Site-Directed Fluorescence Labeling of P-Glycoprotein on Cysteine Residues in the Nucleotide Binding Domains," Biochemistry, 35:11865-11873 (1996)
	*C43	Miller et al., "Peroxide Modifications of Monoalkylated Glutathione Reductase," The Journal of Biological Chemistry, 266:19352-19350 (1991)
	*C44	Nakayama et al., "Chemical Modification of Cysteinyl, Lysyl and Histidyl Residues of Mouse Liver 17β-Hydroxysteroid Dehydrogenase," Biochimica et Biophysica Acta, 1120:144-150 (1992)
	*C45	Nishimura et al., "Reversible Modification of the Sulfhydryl Groups of *Escherichia coli* Succinic Thiokinase with Methanethiolating Reagents, 5,5'-Dithio-bis(2-Nitrobenzoic Acid), p-Hydroxymercuribenzoate, and Ethylmercurithiosalicylate," Archives of Biochemistry and Biophysics, 170:461-467 (1975)
	*C46	O'Connor et al., "Probing an Acyl Enzyme of Selenosubtilisin by Raman Spectroscopy," J. Am. Chem. Soc., 118:239-240 (1996)
	*C47	Pardo et al., "Cysteine 532 and Cysteine 545 Are the *N*-Ethylmaleimide-Reactive Residues of the *Neurospora* Plassma Membrane H^+-ATPase," The Journal of Biological Chemistry, 264:9373-9379 (1989)

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EG	*C48	Peterson et al., "Nonessential Active Site Residues Modulate Selenosubtilisin's Kinetic Mechanism," Biochemistry, 34:6616-6620 (1995)
	*C49	Peterson et al., "Selenosubtilisin's Peroxidase Activity Does Not Require an Intact Oxyanion Hole," Tetrahedron, 53:12311-12317 (1997)
	*C50	Planas et al., "Reengineering the Catalytic Lysine of Aspartate Aminotransferase by Chemical Elaboration of a Genetically Introduced Cysteine," Biochemistry, 30:8268:8276 (1991)
	**C51	Plettner, E., et al., "Modulation of Esterase and Amidase Activity of Subtilisin Bacillus Lentus by Chemical Modification of Cysteine Mutants," Journal of the American Chemical Society, (2 Jun. 1999) 121/21, 4977-4981, XPO000891274.
	**C52	Plettner, Erika et al., "A Combinatorial Approach to Chemical Modification of Subtilisin Bacillus Lentus," Bioorganic & Medicinal Chemistry Letters (Sept. 8, 1998) Vol. 8, No. 17, pp. 2291-2296, XP0004138220
	*C53	Polgar et al., "A New Enzyme Containing a Synthetically Formed Active Site. Thiol-Subtilisin," Journal of American Chemical Society, 88:3153-3154 (1966)
	*C54	Polgar, "Spectrophotometric Determination of Mercaptide Ion, an Activated Form of SH-Group in Thiol Enzymes," FEBS Letters, 38:187-190 (1974)
	*C55	Radziejewski et al., "Catalysis of *N*-Alkyl-1,4-Dihydronicotinamide Ozidation by a Flavopapain: Rapid Reaction in All Catalytic Steps," J. Am. Chem. Soc., 107:3352-3354 (1985)
	*C56	Raia et al., "Activation of *Sulfolobus Solfataricus* Alcohol Dehydrogenase by Modification of Cysteine Residue 38 with Iodoacetic Acid," Biochemistry, 35:638-647 (1996)
	*C57	Ramachandran et al., "Stabilization of Barstar by Chemical Modification of the Buried Cysteines," Biochemistry, 35:8776-8785 (1996)
	*C58	Roberts et al., "Reactivity of Small Thiolate Anions and Cysteine-25 in Papain Toward Methyl Methanethiosulfonate," Biochemistry, 25:5595-5601 (1986)
	*C59	Rokita et al., "Synthesis and Characterization of a New Semisynthetic Enzyme, Flavolysozyme," J. Am. Chem. Soc., 108:4984-4987 (1986)
	*C60	Siddiqui et al., "Arthrobacter D-Xylose Isomerase: Chemical Modification of Carboxy Groups and Protein Engineering of pH Optimum," Biochem. J., 295:685-691 (1993)
	*C61	Smith et al., "An Engineered Change in Substrate Specificity of Ribulosebisphosphate Carboxylase/ Oxygenase," The Journal of Biological Chemistry, 265:1243-1245 (1990)
	*C62	Smith et al., "Chemical Modification of Active Site Residues in γ-Glutamyl Transpeptidase, The Journal of Biological Chemistry, 270:12476-12480 (1995)
	*C63	Smith et al., "Nonessentiality of the Active Sulfhydryl Group of Rabbit Muscle Creatine Kinase," The Journal of Biological Chemistry, 249:3317-3318 (1974)
	*C64	Smith et al., "Restoration of Activity to Catalytically Deficient Mutants of Ribulosebisphosphate Carboxylase/Oxygenase by Aminoethylation," The Journal of Biological Chemistry, 263:4921-4925 (1988)
	*C65	Smith et al., "Simple Alkanethiol Groups for Temporary Blocking of Sulfhydryl Groups of Enzymes," Biochemistry, 14:766-771 (1975)
EG	*C66	Smith et al., "Subtle Alteration of the Active Site of Ribulose Bisphosphate Carboxylase/Oxygenase by Concerted Site-Directed Mutagenesis and Chemical Modification," Biochemical and Biophysical Research Communications, 152:579-584 (1988)

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ED	*C67	Soper et al., "Effects of Substrates on the Selective Modification of the Cysteinyl Residues of D-Amino Acid Transaminase," The Journal of Biological Chemistry, 254:10901-10905 (1979)
	*C68	Stauffer, et al., "Electrostatic Potential of the Acetylcholine Binding Sites in the Nicotinic Receptor Probed by Reactions Of Binding-Site Cysteines with Charged Methanethiosulfonates," Biochemistry, 33:6840-6849 (1994)
	*C69	Stewart et al., "Catalytic Oxidation of Dithiols by a Semisynthetic Enzyme," J. Am. Chem. Soc., 108:3480-3483 (1986)
	*C70	Suckling et al., "Carbon-Carbon Bond Formation Mediated by Papain Chemically Modified by Thiazolium Salts," Bioorganic & Medicinal Chemistry Letters, 3:531-534 (1993)
	*C71	Svensson et al., "Mapping the Folding Intermediate of Human Carbonic Anhydrase II. Probing Substructure by Chemical Reactivity and Spin and Fluorescence Labeling of Engineered Cysteine Residues," Biochemistry, 34:8606-8620 (1995)
	*C72	Valenzuela et al., "Kinetic Properties of Succinylated and Ethylenediamine-Amidated 8-Chymotrypsins," Biochim. Biophys. Acta, 250:538-548 (1971)
	*C73	West et al., "Enzymes as Synthetic Catalysts: Mechanistic and Active-Site Considerations of Natural and Modified Chymotrypsin," J. Am. Chem. Soc., 112:5313-5320 (1990)
	*C74	White et al., "Sequential Site-Directed Mutagenesis and Chemical Modification to Convert the Active Site Arginine 292 Of Aspartate Aminotransferase to Homoarginine," Journal of the American Chemical Society, 114:292-293 (1992)
	*C75	Worku et al., "Identification of Histidyl and Cysteinyl Residues Essential for Catalysis by 5'-Nucleotidase, FEBS Letters, 167:235-240 (1984)
	*C76	Wu et al., "Conversion of a Protease into an Acyl Transferase: Selenolsubtilisin," J. Am. Chem. Soc., 111:4514-4515 (1989)
	*C77	Wynn et al., "Comparison of Straight Chain and Cyclic Unnatural Amino Acids Embedded in the Core of Staphylococcal Nuclease," Protein Science, 6:1621-1626 (1997)
	*C78	Wynn et al., "Mobile Unnatural Amino Acid Side Chains in the Core of Staphylococcal Nuclease," Protein Science, 5:1026-1031 (1996)
	*C79	Wynn et al., "Unnatural Amino Acid Packing Mutants of *Escherichia Coli* Thioredoxin Produced by Combined Mutagenesis/Chemical Modification Techniques," Protein Science, 2:395-403 (1993)
	*C80	Wynn et al., "Chemical modification of Protein Thiols: Formation of Mixed Disulfides," Methods in Enzymology, 251:351-356 (1995)
ED	*C81	Xu et al., "Amino Acids Lining the Channel of the γ-Aminobutyric Acid Type A Receptor Identified by Cysteine Substitution," The Journal of Biological Chemistry, 268:21505-21508 (1993)

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